(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 July 2005 (28.07.2005)

PCT

(10) International Publication Number
WO 2005/068465 A1

(51) International Patent Classification[7]: C07D 475/04, A61K 31/519, A61P 35/00

(21) International Application Number: PCT/US2004/041577

(22) International Filing Date: 10 December 2004 (10.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/534,519 6 January 2004 (06.01.2004) US

(71) Applicants *(for all designated States except US)*: **GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852 (US). **THE PENN STATE RESEARCH FOUNDATION** [US/US]; 304 Old Main, University Park, 16802-7000.

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MOSCHEL, Robert, C.. NELSON, Michael, E.. PEGG, Anthony, E.. LOKTIONOVA, Natalia, A..**

(74) Agent: **PILLAI, Xavier**; Two Prudential Plaza, Suite 4900, 180 N. Stetson Avenue, Chicago, Illinois 60601 (US).

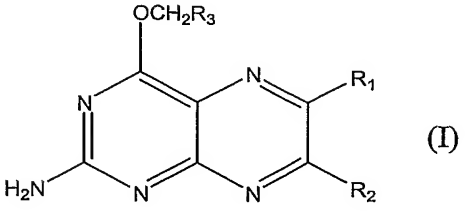
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

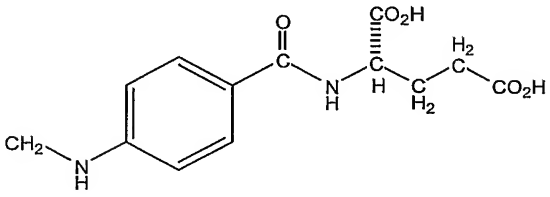
Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 2-AMINO-O4-SUBSTITUTED PTERIDINES AND THEIR USE AS INACTIVATORS OF O6-ALKYLGUANINE-DNA ALKYLTRANSFERASE



(I)



(II)

(57) Abstract: Disclosed are pteridine derivatives of formula (I): (I), wherein, for example, R_1 and R_2 are hydrogen, C_1-C_6 alkyl, carboxyl, formyl, C_1-C_6 hydroxyalkyl, C_1-C_6 carboxyalkyl, C_1-C_6 formyl alkyl, C_1-C_6 alkoxy, acyloxy, acyloxyalkyl wherein the alkyl is C_1-C_6, halogen, or hydroxy, or a group of formula II: (II); and R_3 is (a) phenyl or (b) a cyclic group having at least one 5 or 6-membered heterocyclic ring, optionally with a carbocyclic or heterocyclic ring fused thereto, wherein each heterocyclic ring has at least one hetero atom chosen from O, N, or S; or (c) a phenyl group or a cyclic group, the cyclic group optionally with a carbocyclic or heterocyclic ring fused thereto, which is substituted with 1 to 5 substituents. Disclosed also are pharmaceutical compositions, a method of enhancing the chemotherapeutic effectiveness of cancer treatment agents, a method of deactivating the O^6-alkylguanine-DNA alkyltransferase enzyme, and a method of inhibiting the reaction of O^6-alkylguanine-DNA alkyltransferase enzyme with an alkylated DNA.

WO 2005/068465 A1